CHARGE syndrome

CHARGE syndrome is a disorder that affects many areas of the body. CHARGE stands for coloboma, heart defect, atresia choanae (also known as choanal atresia), retarded growth and development, genital abnormality, and ear abnormality. The pattern of malformations varies among individuals with this disorder, and infants often have multiple life-threatening medical conditions. The diagnosis of CHARGE syndrome is based on a combination of major and minor characteristics.

The major characteristics of CHARGE syndrome are more specific to this disorder than are the minor characteristics. Many individuals with CHARGE syndrome have a hole in one of the structures of the eye (coloboma), which forms during early development. A coloboma may be present in one or both eyes and can affect a person's vision, depending on its size and location. Some people also have small eyes (microphthalmia). One or both nasal passages may be narrowed (choanal stenosis) or completely blocked (choanal atresia). Individuals with CHARGE syndrome frequently have cranial nerve abnormalities. The cranial nerves emerge directly from the brain and extend to various areas of the head and neck, controlling muscle movement and transmitting sensory information. Abnormal function of certain cranial nerves can cause swallowing problems, facial paralysis, a sense of smell that is diminished (hyposmia) or completely absent (anosmia), and mild to profound hearing loss. People with CHARGE syndrome also typically have middle and inner ear abnormalities and unusually shaped ears.

The minor characteristics of CHARGE syndrome are not specific to this disorder; they are frequently present in people without CHARGE syndrome. The minor characteristics include heart defects, slow growth starting in late infancy, developmental delay, and an opening in the lip (cleft lip) with or without an opening in the roof of the mouth (cleft palate). Individuals frequently have hypogonadotropic hypogonadism, which affects the production of hormones that direct sexual development. Males are often born with an unusually small penis (micropenis) and undescended testes (cryptorchidism). External genitalia abnormalities are seen less often in females with CHARGE syndrome. Puberty can be incomplete or delayed. Individuals may have a tracheoesophageal fistula, which is an abnormal connection (fistula) between the esophagus and the trachea. People with CHARGE syndrome also have distinctive facial features, including a square-shaped face and difference in the appearance between the right and left sides of the face (facial asymmetry). Individuals have a wide range of cognitive function, from normal intelligence to major learning disabilities with absent speech and poor communication.

Frequency

CHARGE syndrome occurs in approximately 1 in 8,500 to 10,000 individuals.

Genetic Changes

Mutations in the *CHD7* gene cause more than half of all cases of CHARGE syndrome. The *CHD7* gene provides instructions for making a protein that most likely regulates gene activity (expression) by a process known as chromatin remodeling. Chromatin is the complex of DNA and protein that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. Chromatin remodeling is one way gene expression is regulated during development. When DNA is tightly packed, gene expression is lower than when DNA is loosely packed.

Most mutations in the *CHD7* gene lead to the production of an abnormally short, nonfunctional CHD7 protein, which presumably disrupts chromatin remodeling and the regulation of gene expression. Changes in gene expression during embryonic development likely cause the signs and symptoms of CHARGE syndrome.

About one-third of individuals with CHARGE syndrome do not have an identified mutation in the *CHD7* gene. Researchers suspect that other genetic and environmental factors may be involved in these individuals.

Inheritance Pattern

CHARGE syndrome is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Most cases result from new mutations in the *CHD7* gene and occur in people with no history of the disorder in their family. In rare cases, an affected person inherits the mutation from an affected parent.

Other Names for This Condition

- CHARGE acronym (Coloboma, Heart defect, Atresia choanae, Retarded growth and development, Genital hypoplasia, Ear anomalies/deafness)
- CHARGE association
- Hall-Hittner syndrome

Diagnosis & Management

These resources address the diagnosis or management of CHARGE syndrome:

- GeneReview: CHARGE Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1117
- Genetic Testing Registry: CHARGE association
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265354/

- MedlinePlus Encyclopedia: Choanal atresia
  https://medlineplus.gov/ency/article/001642.htm
- MedlinePlus Encyclopedia: Coloboma
  https://medlineplus.gov/ency/article/003318.htm
- MedlinePlus Encyclopedia: Facial Paralysis
  https://medlineplus.gov/ency/article/003028.htm

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Choanal atresia
  https://medlineplus.gov/ency/article/001642.htm
- Encyclopedia: Coloboma
  https://medlineplus.gov/ency/article/003318.htm
- Encyclopedia: Facial Paralysis
  https://medlineplus.gov/ency/article/003028.htm
- Health Topic: Congenital Heart Defects
  https://medlineplus.gov/congenitalheartdefects.html
- Health Topic: Hearing Problems in Children
  https://medlineplus.gov/hearingproblemsinchildren.html

Genetic and Rare Diseases Information Center

- CHARGE syndrome
  https://rarediseases.info.nih.gov/diseases/29/charge-syndrome

Educational Resources

- Disease InfoSearch: CHARGE Syndrome
  http://www.diseaseinfosearch.org/CHARGE+Syndrome/1315
- Lucile Packard Children's Hospital at Stanford University: Overview of Craniofacial Anomalies
  http://www.stanfordchildrens.org/en/topic/default?id=overview-of-craniofacial-anomalies-90-P01830
- MalaCards: charge syndrome
  http://www.malacards.org/card/charge_syndrome
- My46 Trait Profile
  https://www.my46.org/trait-document?trait=CHARGE%20syndrome&type=profile
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/charge-syndrome/
- Orphanet: CHARGE syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=138
- UC Davis Children's Hospital
  http://www.ucdmc.ucdavis.edu/children/clinical_services/cleft_craniofacial/anomalies/charge.html
- University of Kansas Medical Center
  http://www.kumc.edu/gec/support/charge.html

Patient Support and Advocacy Resources

- AboutFace International
  http://www.aboutface.ca/
- American Association of the Deaf-Blind
  http://www.aadb.org
- CHARGE Syndrome Foundation
  https://www.chargesyndrome.org/
- Children's Craniofacial Association
  http://www.ccakids.com
- DB-Link: The National Consortium on Deaf-Blindness
  https://nationaldb.org/
- Deafblind International
  http://www.deafblindinternational.org/

GeneReviews

- CHARGE Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1117

Genetic Testing Registry

- CHARGE association
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265354/

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28charge+syndrome%5BTIAB%5D%29+OR+%28charge+association%5BTIAB%5D%29+AND+%28choanal+atresia%5BTIAB%5D%29+AND+%28coloboma%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

OMIM

- CHARGE SYNDROME
  http://omim.org/entry/214800

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- GeneReview: CHARGE Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1117
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- Verloes A. Updated diagnostic criteria for CHARGE syndrome: a proposal. Am J Med Genet A. 2005 Mar 15;133A(3):306-8.
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